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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/977,878

10/15/2001

Marsha A. Moses

CMZ-130

3811

50828

7590

05/03/2006

DAVID S. RESNICK

100 SUMMER STREET

NIXON PEABODY LLP

BOSTON, MA 02110-2131

EXAMINER

CANELLA, KAREN A

ART UNIT

PAPER NUMBER

1643

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/977,878	<b>Applicant(s)</b> MOSES ET AL.	
	<b>Examiner</b> Karen A. Canella	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1,2,6,7,9,10,41,42,47 and 48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) 9 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

### DETAILED ACTION

Claim 1 has been amended. Claim 81 has been canceled. Claims 1, 2, 6, 7, 9, 10, 41, 42, 47-48 are pending and under consideration.

Sections of Title 35, U.S. Code not found in this action can be found in a prior action.

The rejection of claims 1, 2, 6, 7, 10, 41, 42, 47 and 48 under 35 U.S.C. 103(a) as being unpatentable over Moses et al (Cancer Research, 1998, Vol. 58, pp. 1395-1399, cited in a previous action) as evidenced by the abstract of Monier et al (Clinica Chimica Acta, Sep 2000, Vol. 299, pp. 11-23) in view of Kjeldsen et al (Journal of Biological Chemistry, 1993, Vol. 268, pp. 10425-10432).

Claim 1 is drawn to a method for facilitating the diagnosis of a subject for a tissue remodeling condition comprising obtaining a urine sample from a subject, contacting said sample with an antibody which specifically binds to NGAL to detect an NGAL/MMP-9 complex, and correlating the presence of the mmp-9/NGAL complex with the presence of a tissue remodeling condition. Claim 2 embodies the method of claim 1 wherein the tissue remodeling associated condition is cancer. Claim 6 embodies the method for claim 2 wherein the cancer is in cells of epithelial origin. Claim 7 embodies the method of claim 6 wherein the cancer is selected from the group consisting of cancers of the nervous system, breast, prostate, retina, lung, skin, kidney, liver, pancreas, genito-urinary tract, and gastrointestinal tract. Claim 10 embodies the method of claim 2 wherein the cancer affects cells of bone or of hematopoietic origin. Claim 41 embodies the method of claim 1 further comprising removal of contaminants from the urine prior to the detection step. Claim 42 embodies the method of claim 41 wherein the urine is dialyzed. Claims 47 and 48 embody the method of claim 1 wherein the MMP-9/NGAL complex is detected by radio-immunoassay or immuno-absorbant assay, respectively. Moses et al teach a method of detecting breast carcinomas by means of detecting high molecular weight complexes comprising MMPs in the urine (Table 2, page 1397 and Figure 1, page 1396) by means of a zymogram containing gelatin (page 1396, under the heading "Data Collection and analysis"). Moses et al teach that the urine was dialyzed before gel electrophoresis (page 1395, second column, lines 8-12 of the section "Sample Preparation and Substrate Gel

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Electrophoresis”, thus fulfilling the specific limitations of claims 41 and 42. Moses et al teach that detection the 125 kDa molecular weight complex in the urine was indicative of breast cancer (page 1396-1397, bridging sentence and page 1398, second column, lines 39-49) which fulfills the specific limitations of claims 6 and 7, and also of claim 10, because breast cancer is metastatic to the bone. Moses et al do not specifically teach the detection of the 125kDa molecular weight complex by means of an anti-NGAL antibody, radio-immunoassay or an immuno-absorbant assay to detect the complex.

The abstract of Monier et al teaches that urine from bladder cancer patients comprised a higher molecular weight complex comprising a 92 kDa protein which is progelatinase-B (MMP-9) in association with NGAL (lines 11-13 of the abstract).

Kjeldsen et al teach an antibody which binds to the 25 kDa protein associated with the 92 kDa gelatinase (page 10425, second column, lines 22-24). Kjeldsen et al teach that the antibody which reacted against the 25 kDa protein, reacted selectively with the 135 kDa form of unreduced gelatinase both by immuno-precipitation and immuno-blotting (page 10428, second column, lines 39-43), which fulfills the specific limitations of claims 47 and 48, regarding the specific type of immunoassay. Kjeldsen et al teach that the identity of the 25 kDa protein is NGAL (page 10431, second column, lines 41-43).

It would have been prima facie obvious at the time the claimed invention was made to obtain urine form a subject and use the anti-NGAL antibody taught by Kjeldsen et al teach to detect the 125 kDa molecular weight complex, wherein detection of said complex is indicative of breast cancer. One of skill in the art would have been motivated to do so by the teachings of the abstract of Monier et al on the isolation of a complex of progelatinase-B (MMP-9) in association with NGAL from the urine of bladder cancer patients; and the teachings of Kjeldsen et al on the anti-NGAL antibody which binds to NGAL in association with the 92 kDa gelatinase and the use of this antibody in immuno-precipitation and immuno-blotting assays for the complex comprising progelatinase-B and NGAL. One of skill in the art would understand that the use of the antibody to detect the complex can substitute for the use of zymography to detect the complex.

The objection of claim 9 as being dependent upon a rejected base claim, but allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims is maintained.

Applicant has submitted a Declaration under 37 CFR 1.131 signed by both inventors averring that prior to August 17, 2000 the molecular species of MMM-9/NGAL was isolated and identified from the urine of cancer patients and recognized by the inventors to be a cancer marker. The evidence presented in the declaration was not persuasive because the autoradiographs are indiscernible. Applicant is requested to provide a photograph with better resolution to replace the gel images of the declaration in order that the evidence of record be clear.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

4/28/2006

  
KARENA. CANELLA PH.D.  
PRIMARY EXAMINER